Establishing a Biospecimen Bank for Research

A biospecimen bank (biobank) is defined as a facility where biological materials (e.g., serum, pathological specimens, genomic material) from human research subjects are stored. The design, operations, material collected, and plans for use and/or sharing for secondary research, determine which regulations apply and the level of IRB review and oversight required.

**Before proposing the establishment of a biobank, research investigators must consider whether the specimens he/she plans to collect would be readily available from a commercial supplier, clinical lab, or an already established research biobank within the institution. Absent scientific justification, the establishment of multiple independent biobanks collecting duplicate material increases the risk of tracking errors due to variability in practices and creates confusion on behalf of participants.**

Comprehensive guidance regarding considerations beyond human subject protections, (e.g., infrastructure requirements, financial resources, facilities, custodianship, personnel training, intellectual property, etc.), is provided in the Reference Section below. This document will focus only on issues related to IRB review and human subject protection.

**IRB Submission of a Biobank Protocol**

The collection, storage, and distribution of human specimens (e.g., blood samples, tissue) for research purposes is subject to IRB review and human subjects research regulations. The IRB is charged with reviewing protocols for obtaining, storing and sharing information, verifying informed consent and protecting privacy and confidentiality. To establish a biobank, the Principal Investigator (PI) submits a Full Review IRB application outlining the collection, storage, and sharing of biospecimens and if applicable, associated information.

Since there is extensive variation in how biobanks operate, the IRB submission should include sufficient information regarding the scientific goals, functions, and operational procedures. The following details are requested, including:

- Justification for establishing a separate bank (e.g., why material cannot be obtained from commercial supplier, clinical repository, or established research bank operating within the institution);
- the purpose of the biobank;
- the material to be collected and stored-
  - leftover discarded tissue from clinical procedures; and/or
  - biospecimens collected as part of research);
- a list of any data that will accompany the specimen or be extracted from the medical record;
- management and physical storage of specimens and data, (e.g., how access secured);
• the type of donors (e.g., minors, adults, healthy participants, patients);
• diagnosis or conditions of study (e.g., specific disease area or broad unspecified use);
• with whom biospecimens will be shared, (e.g., anyone; internal researchers, external collaborators, academic only, commercial industry);
• whether biospecimens will be sold;
• mechanism for how biospecimens will be shared (internally/externally) including procedures for coding, de-identification, encryption data-use agreements, etc.;
• role of an honest-broker* in managing codes and de-identification prior to sharing with recipient researchers;
• management of provisions to protect participant privacy and data confidentiality;
• risks associated with a breach of confidentiality including impact on privacy, insurability, stigmatization etc.;
• the consent process (who obtains, documentation, place, time allotted);
• tracking participant choices where options are provided within the consent;
• length of time a biospecimens will be kept (indefinitely, end of research protocol);
• the ability and procedure for locating/contacting participants (re-consent, incidental findings); participant withdraw procedures;
• the process of re-consent of donors who are minors at the time of donation but turn 18 while the bank is active; and
• whether secondary research could involve genetic or genomic research or creation of cell lines.

*An honest broker is a neutral intermediary (person or system) between the individual whose tissue and data are being studied, and the researcher. The honest broker collects and collates pertinent information regarding the tissue source, replaces identifiers with a code, and releases only coded information to the researcher. An honest broker cannot be study personnel on the protocol or co-author on resulting research publications.

Collectively, these factors provide the IRB with information to be able to determine oversight requirements for both the biobank and if applicable, recipient researchers obtaining material from the biobank for secondary research.

**Biobank Informed Consent/Authorization**

The informed consent and authorization document describes the intended use and procedures for sharing material with others for future research. The purpose may be described as broad and unspecified to allow for a wide range of potential future uses in research. However, even when future use is unspecified, the consent document and process should clearly describe key biobanking concepts such as, unlimited medical record access, incidental findings and obligations to return research results, procedure to withdraw material, large-scale data sharing, etc. so that participants understand the implications of participating.

The UK Informed Consent Template includes sample biobank language. The “Issues to be Addressed and Sample Consent Language for Tissue/Specimen Repositories or Individual Studies Banking Material for Future Use” guide provides points to consider and template
consent language describing risks, protections, and details regarding the collection, storage, and sharing of biospecimens and/or associated data.

**Tracking and Complying with Tiered Consent Options**

If the informed consent for the biobank offers tiered options such as allowing a participant to designate their biospecimen be used only for a specific condition or type of research (e.g., non-genetic testing) then the biospecimens must be tracked and shared accordingly. Tracking requires systems, procedures, and personnel to ensure use matches options selected by the participants.

**Secondary Research Requiring Additional IRB Review**

If the secondary researcher has knowledge of or could ascertain the identity of the biospecimen donor through direct knowledge or associated information, the biospecimen meets the human subject definition and IRB review and approval is required.

IRB review would be required if the recipient researcher (and personnel involved with the secondary research):

- wants to conduct research that goes beyond what is described in the Biobank Informed Consent;
- wants to use specimens in a manner that goes beyond the Biobank Use Agreement;
- needs participant identifiers to track outcomes in the medical record;
- has prior knowledge of the participant through clinical interactions;
- has knowledge of the participant’s surgical procedures in order to obtain fresh tissue for conducting analysis that is sensitive to decay.

IRB review and approval would also be required if biobank personnel wish to collaborate with the recipient researcher on the conduct, analysis, or reporting of the research.

**Secondary Research and Informed Consent**

As part of the review, the IRB would consider the need for a research-specific consent and authorization for any secondary research. Informed consent may not be required if the IRB determines the recipient researcher’s proposed use is consistent with the informed consent for the biobank and the terms of the Biobank Use Agreement.

If use is not consistent, additional consent may be required or the researcher may submit a request to their IRB to alter or waive the requirement for additional consent provided that:

- the secondary research is no greater than minimal risk to participants;
- the waiver will not adversely affect the rights and welfare of the participants;
- the research could not practicably be carried out without the waiver or alteration;
- the participants will be provided with additional pertinent information after participation (if appropriate); and
- secondary research is not bound by other federal, state, or local laws which prohibit waiving or altering informed consent (e.g. NIH Genomic Data Sharing).
However, the requirement for obtaining informed consent would not be waived in cases where the recipient researcher interacts with potential participants or where he/she has an opportunity to obtain informed consent from participants already enrolled in the biobank who have agreed to future contact.

If a secondary researcher has knowledge of the participant’s clinical care or surgical procedure, it will be difficult to justify that research-specific informed consent could not practicably be obtained. Also, other regulatory statutes prohibit the IRB from waiving informed consent, even if specimens are de-identified, (e.g., NIH Funded Genomic Data Sharing or Newborn dried blood spot research).

**Biobank Use Agreement**

Ultimately, secondary research conducted by recipient researchers should be congruent with the uses described in the Biobank Protocol, Biobank Informed Consent Form, and Biobank Use Agreement. The Biobank Use Agreement may include specific limitations based on consent options.

The recipient researcher should be asked to enter into a Biobank Use Agreement which:

- lists biospecimen use limitations, (e.g., consent limited to a specific condition or restriction on research examining ancestry or stigmatizing traits);
- states that the biobank will not share identifiers or the key to coded biospecimens with the recipient researcher;
- specifies that the recipient researcher will not attempt re-identification of biospecimens; and
- prohibits study personnel who operate the biobank from involvement in the conduct or reporting of the secondary research conducted by the recipient researcher (as biobank personnel have access to identifiers).

**Biobank Procedures to Permit Secondary Research without Additional IRB Review (“Not Human Subject” (NHR) determination)**

Biobanks may incorporate procedures that in most cases will allow secondary research to be conducted without additional IRB review based on the fact that the biospecimen no longer meets the regulatory definition of “human subject”. Biobanks may utilize an honest broker to provide researchers with de-identified biospecimens and/or data for secondary research, and may require data use agreements to protect participant confidentiality. Secondary researchers may seek an NHR determination as long as none of the study personnel can readily identify participants who provided the biospecimens.

**Honest Broker Procedures**

The Honest Broker must know the methods (e.g., safe harbor) for de-identification. See the Health & Human Services De-identification instructions for specifics on identifiers and allowable information.
The honest broker retains a code which enables him/her to re-identify a donor should the donor choose to later withdraw, or should it be determined that an actionable result or incidental finding should be returned to the participant (see Return of Research Results Guidance).

**Not Human-Subject Research (NHR) Determination for Secondary Research Project**

The IRB may determine that the secondary research meets the NHR designation and therefore does not require IRB review when de-identification by an honest broker and compliance with the biospecimen use conditions listed above are met. The NHR determination is based on whether the proposed research involves human subjects as described in the sidebar. The recipient researcher submits a description and/or the IRB NHR Determination Form [PDF] to the IRB at IRBSubmission@uky.edu for a determination of whether an activity qualifies as NHR.

**NOT HUMAN-SUBJECT RESEARCH (NHR) DETERMINATION FROM THE IRB**

An IRB may designate secondary research as NHR if the specimen use no longer meets the regulatory definition of human-subject. This involves more than just removal of the 18 HIPAA recognized identifiers. **Human subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. data through intervention or interaction with the individual, or
2. identifiable private information (the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

For examples, see the **UK Guide for Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of NOT HUMAN**.
REFERENCES:

